1: J Clin Oncol. 1998 Apr;16(4):1479-89. Related Articles, Books, LinkOut

Isolated hepatic perfusion with tumor necrosis factor and melphalan for unresectable cancers confined to the liver.

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PURPOSE: To evaluate the efficacy and systemic and regional toxicities of hyperthermic isolated hepatic perfusion (IHP) using tumor necrosis factor (TNF) and melphalan for the treatment of unresectable primary or metastatic cancers confined to the liver. PATIENTS AND METHODS: Thirty-four patients (18 men and 16 women; mean age, 49 years) underwent a 60-minute hyperthermic (39.5 degrees to 40.0 degrees C) IHP performed by laparotomy that used TNF 1.0 mg and melphalan 1.5 mg/kg. Perfusion inflow was through the gastroduodenal artery and outflow was from a cannula positioned in an isolated segment of retrohepatic inferior vena cava (IVC). Infrahepatic IVC and portal venous blood flow were shunted to the axillary vein using an external venoveno bypass circuit. Complete vascular isolation of the liver was confirmed by an I-131-labelled human serum albumin monitoring technique. RESULTS: There was no operative mortality. Seventy-five percent of patients had reversible grade III or IV (National Cancer Institute Common Toxicity Criteria) hepatic toxicity with one treatment-related mortality (3%) because of hepatic venoocclusive disease. In 33 assessable patients, the overall response rate was 75% (complete response, one patient [3%]; partial response, 26 patients [72%]). With a median potential follow-up of 15 months, the mean duration of response was 9 months (range, 2 to 30 months). CONCLUSION: IHP with TNF and melphalan results in significant regression of bulky hepatic cancers confined to the liver in the majority of patients. Based on these initial results, further refinement of this treatment technique is warranted; perhaps by the combination of IHP with other regional treatment strategies to provide long-term control of unresectable cancers confined to liver.

Publication Types:

- Clinical Trial
- Clinical Trial, Phase II

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Help

1: Arch Surg. 1999 Mar;134(3):303-7. Related Articles, Books, LinkOut

Hyperthermic isolated limb perfusion with tumor necrosis factor alpha, interferon gamma, and melphalan for locally advanced nonmelanoma skin tumors of the extremities: a multicenter study.

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BACKGROUND: Hyperthermic isolated limb perfusion (HILP) with tumor necrosis factor alpha (TNF-alpha), interferon gamma, and melphalan has proved to be useful in the treatment of recurrent malignant melanoma and of locally advanced soft tissue sarcomas of the extremities. OBJECTIVE: To determine whether this modality is also effective in the treatment of locally advanced nonmelanoma skin tumors of the extremities. PATIENTS AND METHODS: Fifteen patients with locally advanced primary, recurrent, or metastatic skin tumors of the extremities (12 with squamous cell carcinoma and 3 with Merkel cell carcinoma) underwent HILP with TNF-alpha, interferon gamma, and melphalan. Six tumors were localized in the upper extremity (40%), and 9 in the lower extremity (60%). Treatment-related complications, limb salvage rate, local recurrence, and regional and distant metastases were scored during a median follow-up of 20 months. RESULTS: After HILP, 9 patients (60%) showed a complete response (with histopathological confirmation). Four patients (27%) showed a partial response (with histopathological confirmation in 1 patient), and 2 patients (13%) showed no change (with histopathological confirmation in 1 patient and with clinical evidence in 1 patient). Two patients (13%) showed treatment-related complications. The limb salvage was achieved in 12 patients (80%), and the local recurrences developed in 4 patients (27%). During follow-up, regional lymph node metastases were observed in 2 patients (13%) and distant metastases in 2 patients (13%). CONCLUSION: Based on our results, HILP with TNF-alpha, interferon gamma, and melphalan should be considered as a limb-saving treatment modality in patients with locally advanced nonmelanoma skin tumors of the extremities who would otherwise be candidates for ablative surgery.

Publication Types:
- Clinical Trial

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Help

1: Arch Surg. 1999 Feb;134(2):177-80. Related Articles, Books, LinkOut

Isolated limb perfusion with high-dose tumor necrosis factor alpha and melphalan for Kaposi sarcoma.

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BACKGROUND: Although the classic form of Kaposi sarcoma is considered indolent and benign, at times its evolution is more severe, with an acute onset and debilitating complications necessitating aggressive treatment and even amputation. OBJECTIVE: To evaluate the efficacy of hyperthermic isolated limb perfusion (ILP) with tumor necrosis factor alpha and melphalan as a limb-sparing modality for extensive regional Kaposi sarcoma. SETTING: University hospital and national referral center. PATIENTS: Five patients, aged 60 to 82 years, with extensive, symptomatic, classic Kaposi sarcoma of the lower limb were operated on. All were candidates for amputation owing to debilitating symptoms. INTERVENTIONS: Patients underwent ILP through the iliac (n = 2), femoral (n = 2), and popliteal (n = 1) vessels. Tumor necrosis factor alpha, 4 mg, and melphalan, 1.5 mg/kg body weight, were perfused for an overall time of 90 minutes. The limb was heated to 40 degrees C. Clinical and pathological responses were recorded for all patients after 6 to 8 weeks. RESULTS: The overall response rate was 100%: 1 of 5 patients had complete response and 4 of 5 had partial response. Two patients had progression of disease 2 months after ILP but one of them was asymptomatic and did not require any further treatment. The second patient underwent amputation. Thus, limb preservation was achieved in 80% (4 of 5 patients). Median follow-up was 24 months. There were no deaths associated with treatment or major system complications. Local complications were all reversible. CONCLUSION: These findings suggest that hyperthermic ILP with tumor necrosis factor alpha and melphalan can be considered an effective palliative and limb-sparing treatment modality for extensive Kaposi sarcoma.

Publication Types:
- Clinical Trial

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Help

1: Ann Surg. 1996 Dec;224(6):756-64; discussion 764-5.

Isolated limb perfusion with tumor necrosis factor and melphalan for limb salvage in 186 patients with locally advanced soft tissue extremity sarcomas. The cumulative multicenter European experience.

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OBJECTIVE: The objective of the study was to achieve limb salvage in patients with locally advanced soft tissue sarcomas that can only be treated by amputation or functionally mutilating surgery by performing an isolated limb perfusion (ILP) with tumor necrosis factor (TNF) + melphalan (M) as induction biochemotherapy to obtain local control and make limb-sparing surgery possible. SUMMARY BACKGROUND DATA: To increase the number of limb-sparing resections in the treatment of locally advanced extremity soft tissue sarcoma, preoperative radiation therapy or chemotherapy or a combination of the two often are applied. The ILP with cytostatic agents alone is another option but rarely is used because of rather poor results. The efficacy of the application of TNF in ILP markedly has changed this situation. METHODS: In 8 cancer centers, 186 patients were treated over a period of almost 4.5 years. There were 107 (57%) primary and 79 (43%) recurrent sarcomas, mostly high grade (110 grade III; 51 grade II; and 25 very large, recurrent, or multiple grade I sarcomas). The composition of this series of patients is unusual: 42 patients (23%) had multifocal primary or multiple recurrent tumors; median tumor size was very large (16 cm); 25 patients (13%) had known systemic metastases at the time of the ILP. Patients underwent a 90-minute ILP at 39 to 40 C with TNF + melphalan. The first 55 patients also received interferon-tau. A delayed marginal resection of the tumor remnant was done 2 to 4 months after ILP. RESULTS: A major tumor response was seen in 82% of the patients rendering these large sarcomas resectable in most cases. Clinical response rates were: 33 complete response (CR) (18%), 106 partial response (PR) (57%), 42 no change (NC) (22%), and 5 progressive disease (PD) (3%). Final outcome was defined by clinical and pathologic response: 54 CR (29%), 99 PR (53%), 29 NC (16%), and 4 PD (2%). At a median follow-up of almost 2 years (22 months; range, 6-58 months), limb salvage was achieved in 82%. Regional toxicity was limited and systemic toxicity minimal to moderate, easily managed, with no toxic deaths. CONCLUSIONS: In the setting of isolated limb perfusion, TNF is an active anticancer drug in patients. The ILP with TNF + melphalan can be performed safely in many centers and is an effective induction treatment with a high response rate that can achieve limb salvage in patients with locally advanced extremity soft tissue sarcoma.

Publication Types:

- Clinical Trial
- Multicenter Study

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